REMARKS

By the current amendment claims 29, 32, 34, 37, 40, 70, 72, and 77 are amended; claim 74 is cancelled. Claims 29-40, 70-73 and 75-77 are now pending. The Applicants respectfully request the Examiner to reconsider the rejections in view of amendments to the claims now presented and the following remarks.

Specification Objection

The Office Action objects to the Specification at page 49, line 27 as containing sequence disclosures not identified by sequence identifier numbers. Applicants have previously addressed this objections to the specification in the Preliminary Amendment filed on August 16, 2002. In that Amendment, "SEQ ID NO 1" was inserted in the position identified in the Office Action. Examiner is respectfully requested to withdraw all outstanding objections to the now pending claims.

Rejections under 35 U.S.C. §112, first paragraph

The Office Action has alleged that the subject matter of the claims is indefinite under 35 U.S.C. § 112, first paragraph. The Office Action alleges that the Applicant's failed to respond to this rejection in the last response. The Applicants in their last response pointed out that Examples of polynucleotides are listed at page 48 of the specification. Compositions comprise, for example, at least one gene expressing the antigen and a gene expressing the molecule that can activate dendritic cells or other antigen presenting cells and thus can serve as adjuvant (p. 48 lines 24-28). The examples of adjutants are presented on p. 48 line 28 to p. 50, line 8). Importantly, the genes driven by NFkB or CMV promoter are preferred. (It important to know also that CMV promoter ALSO contains the NFkB element). At the same time constructs under SV-40 promoter it activated by the formulation to my less extent, while genes under AP-1-sensitive cassette are not activated (see Example 62) as well as p. 49, line 6 to p. 50 line 8.

The Applicants therefore respectfully request the Examiner to withdraw the rejections under U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. §102(e)

Claims 29-40 and 70-77 stand rejected under 35 U.S.C 102(e) as being anticipated by Manthorpe et al. (US 2002/0,019,358). The Applicants have now amended the claims to recite

that more than one plasmid or gene is expressed, and wherein at least one expresses an antigen and at least one expresses a molecule that activates dendritic cells. The Examiner is particularly referred to page 48, line 24, *et seq.*, to p. 49, line 5 of the instant Specification where the Applicants teach that more than one polynucleotide is preferably expressed.

In contrast Manthorpe et al., '358 does not disclose or suggest the invention as currently claimed. In fact, in discussing the prior art (Manthorpe et al. '358), a previous Office Action indicated that "it is unknown . . . that any polynucleotide would induce an immune response and activate Dendritic cells . . . " See March 23, 2004 Office Action, page 8. This statement, while made in a §112 rejection illustrates the state of the art with respect to the claimed invention, and precludes an anticipation rejection.

Rejections under 35 U.S.C. §103(a)

Claims 29, 31-32, 34, 36-37, 39-40, 70, 72, and 74-77 stand rejected under 35 U.S.C. §103 as obvious over Carson et al. (US 5,830,877), in view of Kabanov et al. (US 5,656,611). This rejection is traversed.

As indicated above, the Applicants have now amended the claims to recite that more than one plasmid or gene is expressed, and wherein at least one expresses an antigen and at least one expresses a molecule that activates dendritic cells. Neither Carson et al. '877 nor Kabonav et al. '611 teach or suggest this feature alone or in combination.

Both Carson et al. '877 *and* Kabanov et al. '611 stress and teach toward cationic entities to merely effect of nucleic acid delivery, not teach formulations for the administration of nucleic acids *or* for the activation of dendritic cells, and not wherein more that one plasmid or gene is expressed. Enhanced ability of nucleic acids to cross cell membranes does not result in the enhanced activation of dendritic cells, and the Office Action does not address this issue. In fact, as indicated above, the previous Office Action's assertion that "it is unknown . . . that any polynucleotide would induce an immune response and activate Dendritic cells. . ." The invention as currently claimed achieves unexpected results in an art that "lacks predictability". See March 23, 2004 Office Action, page 8.

Further Rejections under 35 U.S.C. §103

Claims 30, 33, 35, 38, 71, and 73 stand rejected under 35 U.S.C. §103 as obvious over Carson et al., '877 or Mathiowitz et al. (US 6,677,313), and Kabanov et al., '611 as applied to claims 29, 31-32, 34, 36-37, 39-40, 70, 72, and 74-77, further in view of Alakhov et al. (US 6,218,438) or Kabanov et al. (US 6,387,406) or Manthorpe et al. '358).

For an obviousness rejection, the motivation to combine the references must be present to solve the same problem, i.e., to induce activation of dendritic cells. Moreover, most importantly with regard to the facts of the claims presented, all the limitations of the instant claims must be found within the prior art references to render the claimed subject matter *prima facie* obvious. In this case none of the prior art references disclose more than one plasmid or gene is expressed, and wherein at least one expresses an antigen and at least one expresses a molecule that activates dendritic cells. Morevoer, there is no motivation to combine or modify the listed references to achieve the invention as presently claimed.

The nucleic acid contemplated by Raz et al. (US 6,589,940) is not equivalent or comparable to an adjuvant or antigen defined within the scope of the instant written description and presented claims.[1] Moreover, the Raz et al. '940 disclosure does not contemplate, suggest, or describe the critical formulation. i.e., polyoxyethylene-polyoxypropylene block co-polymers. The Kabanov et al. '611 disclosure particularly teaches and stresses the advantages of polycationic polyether block copolymers compositions to increase the ability of nucleic acids to cross cell membranes; however, the Kabanov et al. '611 disclosure does not contemplate, suggest, or describe any method of inducing the activation of dendritic cells *or* any method of modulating an immune response. Both Carson et al. '877 *and* Kabanov et al. '611 stress and teach toward *cationic entities* to merely effect of nucleic acid delivery. Kabanov et al. '438 does not teach formulations for the administration of nucleic acids *or* for the activation of dendritic cells.

Accordingly, the Applicants respectfully request the Examiner to withdraw the rejections under 35 U.S.C. §103.

---

[1] Although Raz, *et al.*, contemplate the administration of an oligonucleotide sequence, column 4, line 34, for example, the entire contemplated entity is composed of about 8 nucleotides.

Obviousness-Type Double Patenting Rejection

The Applicants respectfully submit that the double patenting issues are each moot in view of amendments to the claims presented herewith. The Applicants, in any event, elect to defer resolution of this issue until the final scope of the pending claims is determined. The Applicants' indeed, however continue to acknowledge their willingness to execute a terminal disclaimer under 37 CFR §1.321(c) if necessary.

For all the foregoing reasons, the Applicants submit that Claims 29-40 and 70-77 are in condition for allowance. The Examiner is kindly encouraged to telephone the undersigned in order to expedite any detail of the prosecution.

The Commissioner is authorized to charge any deficiency or credit any overpayment in connection herewith to Deposit Account No. 13-2165.

In view of the foregoing, Applicants submit that all pending claims are in condition for allowance and request that all claims be allowed. The Examiner is invited to contact the undersigned should she believe that this would expedite prosecution of this application. It is believed that no fee is required. The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,

Dated: March 22, 2005

Christopher S. Casieri
Reg. No. 50,919
Attorney for Applicants

MATHEWS, COLLINS, SHEPHERD & McKAY, P.A.
100 Thanet Circle, Suite 306
Princeton, NJ 08540
Tel: 609 924 8555
Fax: 609 924 3036